ANTINUCLEAR AND ASSOCIATED AUTO-ANTIBODIES IN PATIENTS WITH OPTIC NEURITIS SECONDARY TO NEUROMYELITIS OPTICA SPECTRUM DISORDER

AUTHOR: **PULKIT GUPTA**

AFFILIATION: SALISBURY NHS FOUNDATION TRUST, SALISBURY, UNITED KINGDOM

INTRODUCTION:

First identified in 1894, 'neuro-myélite optique aiguë'/Devic's disease was renamed as NeuroMyelitis Optica Spectrum Disorder (NMOSD) in 2015. It is well established that optic neuritis (ON) is one of the three absolute diagnostic criteria for NMOSD; with positive Aquaporin-4 (AQP4) antibodies. Alternately, cases of ON secondary to connective tissue disorders (CTD) with positive autoantibodies have also been reported, with or without positive AQP4. [1-4]

METHODS:

We came across three patients (A, B, C) who presented with unilateral visual loss secondary to retrobulbar ON. The ages of these two females and one male (B) ranged between 26 to 43 years, and their visual acuities at presentation were perception of light (A), 1.2 logMAR (B), and no perception of light (C). Blood assessment indicated positive AQP4 antibodies in all three.

Additional flagged blood results:

Patient A: Syphilis Total Antibody, positive Anti-nuclear (ANA), Anti-Ro, Anti-RNP antibodies. This led to an initial incidental diagnosis of partially treated syphilis in the past, or a reinfection; but the CSF analysis returned as unremarkable with no clinical evidence to indicate asymptomatic, meningeal, meningo-vascular, or parenchymal Neurosyphilis.

Patient B: Positive ANA, Anti-Ro antibodies.

Patient C: Elevated IgG-DS DNA, positive ANA antibodies.

Unremarkable lupus, anti-cardiolipin and vasculitis screen in all three.

RESULTS:

A,B,C received Intravenous methylprednisolone (IVMP) 1 gm pulsed over 3 days followed by oral prednisolone and exhibited visual recovery: (A) 1.3 log MAR; 0.32 (B); 0.28 (C) between 3-6 weeks follow-up.

CONCLUSION:

All three of our patients exhibited positive AQP4 and responded to IVMP. Other than elevated auto-antibodies, there was no evidence to suggest associated CTD, or infection. Until the time of this submission, the ON was conclusively considered to be secondary to NMOSD in all three patients.

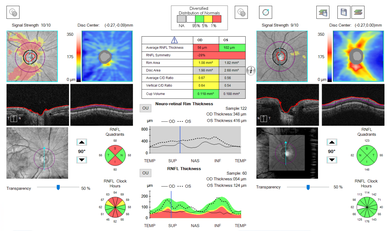
DISCUSSION:

AQP4 antibodies are positive in 8/10 cases of NMOSD owing to the perivascular deposition of IgG and activated complement, loss of astrocytic AQP4, inflammatory infiltration with macrophage accumulation and demyelination with axon loss. Additionally, patients with NMO or MS may exhibit accompanying autoantibodies and autoimmune diseases eg. SS, ANA, extractable nuclear antigen antibodies (SSA/SSB), rheumatoid factor (RF), anticardiolipin antibodies (ACA), and anti-double-stranded DNA antibody (A-ds DNA). [2,3,5-6]

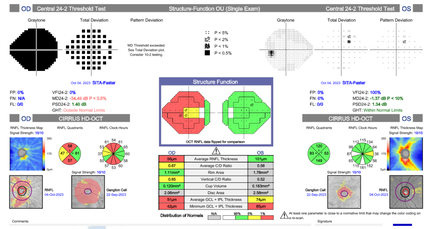
Optic nerve involvement in Syphilis may be unilateral/bilateral and manifest as perineuritis, anterior or retrobulbar ON or papilloedema. However, a diagnosis of Syphilis cannot be confirmed in the presence of unremarkable CSF analysis or no clinical evidence. [7]

As per the American College of Rheumatology's proposed criteria for neuro-psychiatric SLE, 12 syndromes (involving CNS and optic nerve) may be observed in 3.6% cases of SLE. The most common is optic neuritis, followed by myasthenia gravis, visual field defects, and Idiopathic Intracranial Hypertension. The primary SS related (anti-Sjögren syndrome A (SSA), anti-Sjögren syndrome B) optic neuritis is rare, but it has been associated with NMOSD. Studies indicate that patients with CNS involvement associated with CTDs exhibit limited response to conventional therapies. However, a diagnosis of CTDs cannot be confirmed in the absence of mucocutaneous, musculoskeletal, or haematological and reticuloendothelial manifestations OR Negative/unremarkable Lupus, anti-cardiolipin and vasculitis screen. [5,6]

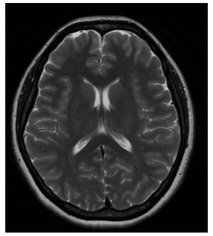
Patient A- OCT RNFL



Patient A HFA 24-2



Patient C- MRI



REFERENCES:

1. Devic E. Congrès français de médecine (Premiere Session; Lyon, 1894; procès-verbaux, mémoires et discussions; publiés par M. le Dr L. Bard) Paris: Lyon: Asselin et Houzeau, Louis Savy; 1895. Myélite aiguë dorso-lombaire avec névrite optique. - Autopsie; pp. 434–439.
2. Jarius S, Wildemann B. The history of neuromyelitis optica. J Neuroinflammation. 2013 Jan 15;10:8.
3. Levin MH, Bennett JL, Verkman AS. Optic neuritis in neuromyelitis optica. Prog Retin Eye Res. 2013;36:159-71.
4. Li H, Zhang Y, Yi Z, Huang D, Wei S. Frequency of autoantibodies and connective tissue diseases in Chinese patients with optic neuritis. PLoS One. 2014 Jun 20;9(6).
5. Zahid S, Iqbal M. Systemic Lupus Erythematosus Presenting as Optic Neuropathy: A Case Report. Cureus. 2019 Jun 3;11(6).
6. Tang WQ, Wei SH. Primary Sjögren's syndrome related optic neuritis. Int J Ophthalmol. 2013 Dec 18;6(6):888-91.
7. Smith GT, Goldmeier D, Migdal C. Neurosyphilis with optic neuritis: an update. Postgrad Med J. 2006 Jan;82(963):36-9.